Laboratory for Doping Control and Metabolic Studies

Personnel (as of 31/12/2021):

- Dimitris Kletsas, Institute Director, Laboratory Administrative Director
- Argyro Fragkaki, PhD Chem, Laboratory Scientific Director
- Aimilia Makrygianni, MSc Chem, Quality Manager
- Ioannis Angelis, PhD Chem, Analyst
- Athanasia Kioukia-Fougia, PhD Pharm, Analyst
- Polyxeni Kiousi, PhD Chem, Analyst
- Christoforidis Christoforos, PhD Chem, Analyst
- Olga Goula, Chemist, MSc student, Analyst
- Paraskevopoulou Katerina, Chem Eng, PhD student, Analyst

- Sakellariou Panagiotis, PhD Biol, Analyst
- Tsimelis Efstathios, Med Technol, PhD student, Analyst
- Fotini Chlapana, Technician
- Stella Loui, Technician
- Maria Fillipidou, Secretary
- Maria Vlachou, Secretary
- Maria Pavlaki, Support personnel
- Vassiliki Tzouvara, Support personnel

Laboratory Description

The Doping Control Laboratory of Athens (DCLA) was founded in 1986 and is located in the Olympic Athletic Center of Athens (OAKA) complex in a dedicated 3-floor building, built for the doping control testing of the 2004 Olympic Games. Since January 2019, it has been decided to become a Central Service Facility of IBA and the transfer was finalized within 2020.

The infrastructure of DCLA includes state-of-the-art analytical instrumentation, including GC (2), GC/MS (5), GC/C/IRMS, GC/TOF/MS, LC/TOF/MS, GC/HRMS (3), ALS (14), UHPLC-OrbitrapMS (2), hematological analyzer, etc.

DCLA was accredited by the International Olympic Committee (IOC) in 1995 and later (in 2000) by ESYD, the Greek accreditation body, according to the requirements of the International Standard ISO/IEC 17025. DCLA was also accredited by the World Anti-Doping Agency (WADA) in the field of the anti-doping testing in humans as well as it is accredited by the Association of Official Racing Chemists (AORC) in the field of the anti-doping testing in horses.

DCLA performed the doping control of the World Championships in Athletics in Athens (1997), of the 28th Summer Olympic Games in Athens (2004) and of the Mediterranean Games of Mersin, Turkey (2013). It has also analyzed samples of many National Anti-Doping Organizations (NADOS), ADOs and International Federations (IFs), such as the Greek NADO, Cyprus Anti-Doping Agency (CYADA), Tunisian Anti-Doping Agency, Israel NADO, Turkish Anti-Doping Committee, UEFA, FIBA, National Anti-Doping Commission of Albania, Federation Internationale de Volleyball (FIVB), Union Cycliste Internationale (UCI), Portugal NADO, Anti-Doping Centre of Bulgaria, National Anti-Doping Organisation of Malta. In the field of equine samples analyses, DCLA has analyzed samples from the Jockey Club of Greece and the Hellenic Equestrian Federation.

The members of the scientific staff have attended international meetings and symposia, such as the Manfred Donike Workshops in the Anti-Doping Science and the U.S. Anti-Doping Agency (USADA) Symposium as well as they have participated as international experts in the 20th Winter Olympic Games in Torino, Italy (2006), the 30

Summer Olympic Games in London, UK (2012), the 22

Winter Olympic Games in Sochi, Russia (2014), the 31 st

Summer Olympic Games in Rio de Janeiro, Brazil (2016) and the 32 $_{\mbox{\scriptsize nd}}$

Summer Olympic Games in Tokyo, Japan (2021).

DCLA has undertaken several research programmes in the anti-doping research, either partially funded by the WADA or anti-doping organizations, such as CYADA or exclusively funded by the former host organization (OAKA). The results of these projects have been published in peer-reviewed journals and were presented in international anti-doping workshops. The lists below provide information regarding the most recent research programmes conducted by DCLA as well as the most recent scientific publications in the field of anti-doping research. In addition, many dissertation theses either for MSc or PhD studies have been conducted in the premises of the DCLA with its scientific members as supervisory staff in cooperation with local universities.

In the previous years, DCLA was analyzing annually more than 3,000 urine and blood samples for sport drug testing according to the WADA International Standard for Laboratories (ISL). It was participating in all WADA external quality control and double blind rounds as per ISL and has host external assessments from WADA laboratory expert teams. Currently, DCLA is in the process to restore the WADA accreditation. In parallel, the Laboratory is accredited by the Association of the Official Recing Chemists (AORC) and provides anti-doping testing control for the Hellenic Equestrian Federation. Finally, IBA has recently signed a Memorandum of Understanding with the Cyprus Anti-doping Agence for a scientific collaboration between the two parties.

DCLA was always interested in the development of scientific research in the field of doping control and strengthening of these activities is among the future goals of the laboratory. Furthermore, according to the WADA requirements the Laboratory must devote a part of its activities in research. It is anticipated that the recently established connection between the DCLA and the Laboratories of IBA provides new opportunities for common research projects mainly in the fields of the characterization of newly developed molecules, toxicity studies, anti-ageing approaches and enhancement of biological performance, as well as drug and environmental analyses. This interaction will combine the excellent infrastructure and expertise of DCLA for in the characterization of molecules and in metabolic and proteomic studies with the cell based and animal studies of the rest of the IBA Laboratories. Several new projects in this direction are already ongoing.

List of recent research projects D

Funded by World Anti-Doping Agency (WADA)

2021-ongoing: Synthesis of the main long-term dihydroxylated metabolite of LGD-4033 as reference material for doping control analysis (Reference Number: 21A17EP)

Participants: Doping Control Laboratory of Athens and NCSR "Demokritos"

2017-ongoing: Chemical derivatization of intact phase II metabolites of Anabolic Androgenic Steroids (AAS) for confirmatory purposes.

Participants: Doping Control Laboratory of Athens

2012-2017: Detection of sulfo-conjugated anabolic steroids metabolites in Antidoping initial and confirmatory analysis.

Participants: Doping Control Laboratory of Athens

2013-2014: Development and harmonisation of direct quantitative urinalysis methods for threshold substances.

Participants: coordinated by the Doping Control Laboratory of Ghent and in collaboration with the Doping Control Laboratories of Athens, Barcelona, Sydney, Bloemfontein.

2015-2020: Pharmacokinetics of inhaled salmeterol alone or in combination with fluticasone and investigation of the role of CYP3A4 and P-gp polymorphisms.

Participants: Coordinated by the University of Nicosia and in collaboration with the Cyprus Institute of Neurology and Genetics and Doping Control Laboratory of Athens.

List of Recent Peer-Reviewed Publications

1. Wagener F, Guddat S, Gorgens C, Angelis YS, Petrou M, Lagojda A, Kuhne D, Thevis M. (2021). Investigation into the elimination profiles and metabolite ratios of micro-dosed selective androgen receptor modulator LGD-4033 for doping control purposes. Anal Bianal Chem. doi.org/10.1007/s00216-021-03740-7.

2. Kiousi P, Fragkaki AG, Kioukia-Fougia N, Angelis YS (2021). Liquid chromatography-mass spectrometry behavior of Girard's T derivatives of oxosteroid intact phase II metabolites for doping control purposes. Drug Test Anal. doi: 10.1002/dta.3056.

3. Sakellariou P, Kiousi P, Fragkaki AG, Lyris E, Petrou M, Georgakopoulos C, Angelis YS. (2021). Alternative markers for methylnortestosterone misuse in human urine. Drug Test Anal. doi: 10.1002/dta.2887.

4. Fragkaki AG, Petropoulou G, Athanasiadou I, Kiousi P, Kioukia-Fougia N, Archontaki H, Bakeas E, Angelis YS. (2020). Determination of anabolic androgenic steroids as imidazole carbamate derivatives in human urine using liquid chromatography-tandem mass spectrometry. J. Sep. Sci. doi: 10.1002/jssc.202000036.

5. Chajistamatiou A, Angelis Y, Kiousi P, Tsivou M. Bakeas E. (2019). Discrimination of tetryl samples by gas chromatography - isotope ratio mass spectrometry. <u>Forensic</u>

12:42-45.

6. <u>Fragkaki</u> AG, <u>Sakellariou</u> P, <u>Kiousi</u> P, <u>Nassia Kioukia-Fougia</u> N, <u>Tsivou</u> M, <u>Petrou</u> M,

<u>Angelis</u> Y (2018). Human *in vivo* metabolism study of LGD-4033. Drug Test Anal. doi:10:1635-1645.

7. <u>Abushareeda W, Vonaparti A.</u>, <u>Al Saad</u> K, Almansoori M, <u>Meloug</u> M, <u>Saleh A, Aguil</u> <u>era R,</u> Angelis Y,

Horvatovich PL,

Lommen A, Alsayrafy

Μ,

Georgakopoulos

C (2018). High resolution full scan liquid chromatography mass spectrometry comprehensive screening in sports antidoping urine analysis.

J. Pharm. Biomed. Analysis

151:10-24.

8. Fragkaki AG, Kioukia-Fougia N, Kiousi P, Kioussi M, Tsivou M. (2017). Challenges in detecting substances for equine anti-doping. Drug Test Anal. doi:10.1002/dta.2162.